



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit : 1615
Examiner : Amy E. Pulliam
Serial No. : 09/648,304
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Inventor(s) : Airton Monza da Silveira

Customer No. 03581

Docket No.: 1369-0

Confirmation No.: 6411

: Gilles Ponchel
: Dominique Duchene
: Patrick Couvreur
: Francis Puisieux
Title : NANOPARTICLES COMPRISING AT LEAST
: ONE POLYMER AND AT LEAST ONE
: COMPOUND ABLE TO COMPLEX ONE OR
: MORE ACTIVE INGREDIENTS

Dated: October 7, 2003

RESPONSE

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is submitted in response to the Official Action dated April 7, 2003.

The Applicants acknowledge the continued rejection of Claims 1, 2 and 4 – 13 over the hypothetical combination of Trinh with Chen as being *prima facie* obvious.

The Applicants note with appreciation the Examiner's detailed and helpful comments supporting the hypothetical combination, irrespective of the deficiencies of the primary reference, namely, Chen, which necessitates the combination. The Applicants maintain their position that one of ordinary skill in the art would not make the hypothetical combination as suggested in the Official Action. Those reasons have been set forth in detail in earlier amendments.

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Response

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However, the Applicants respectfully submit that it makes no difference if the teachings of Trinh with respect to cyclodextrin complexes are combined with the disclosure of Chen (ionic polymer matrix + active compound + metal ion). The reason that it makes no difference is that, even if one of ordinary skill in the art were to make the hypothetical combination as set forth in the Official Action, the resulting product of the combination would still fail to teach or suggest the invention as recited in the solicited claims.

Independent Claim 1, for example, recites (among other things) that the active ingredient is largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles. Chen inherently cannot provide such teachings or suggestions since Chen admittedly does not teach cyclodextrins as a complexing agent at all.

That leaves consideration of Trinh. Trinh concerns an hydrophobic complex between cyclodextrin and an active ingredient. However, careful scrutiny of the entire Trinh disclosure reveals that there is not a single word concerning the fact that a cyclic oligosaccharide could be utilized in conjunction with a polymer and an active ingredient such that the active ingredient is largely contained in the nanoparticle matrix network and that the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles.

In fact, the Applicants respectfully submit that Trinh teaches quite the opposite. Trinh provides teachings and suggestions that would lead one of ordinary skill in the art to expect that the hydrophobic active ingredient would only be entrapped in the cyclodextrin molecules. Unfortunately, that is not what the Applicants claim. Instead, the Applicants claim that the active ingredient is largely contained in the nanoparticle matrix network while the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles. Trinh simply fails to teach or suggest this.

As a consequence, even if one of ordinary skill in the art were to make the hypothetical combination as suggested in the Official Action, there is utterly no expectation by those of ordinary skill in the art that the resulting product would have the active ingredient largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules located on the surface of the nanoparticles. In sharp contrast, the Applicants are the ones that unexpectedly discovered this. Those of ordinary skill in the art, based on the teachings of Trinh and Chen, would have had the reasonable expectation that the active ingredient would stay entrapped in the cyclodextrin molecules and not react with the ionic polymer matrix disclosed by Chen, as Chen teaches the ionic interaction between the ionic polymer matrix, the active ingredient and the metal ion. The Applicants surprisingly discovered that this is not the case and there is utterly no disclosure, no teachings and no suggestions in either or both of Trinh and Chen that this could or would happen.

The Applicants accordingly respectfully submit that, not only is the hypothetical combination not *prima facie* obvious, but that the hypothetical combination is non-enabling. Specifically, the hypothetical combination is non-enabling with respect to the portion of the Applicants' claims that recite that the active ingredient is largely contained in a nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles.

The Applicants note that the outstanding Official Action does not address this particular aspect of the claims, despite the fact that the claimed language concerning the active ingredient being largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules were localized on the surface of the nanoparticles was present in the last amendment and entered into the Official Record. This is an important aspect of the invention that must be

addressed and considered on the merits, irrespective of the finality of this Action. The simple fact is that both of Chen and Trinh do not disclose, teach or suggest this specifically and affirmatively claimed aspect of the invention. Withdrawal of the rejection based on that hypothetical combination of disclosures is accordingly respectfully requested.

The Applicants also acknowledge the rejection of Claims 1, 2 and 4 – 26 over the hypothetical combination of Trinh with Ramtoola.

Trinh suffers the same deficiencies set forth in detail above. Ramtoola discloses ionic reactions between a polymer (polyalkylcyanoacrylate polymer) and an active ingredient which is insulin at low pH ($\text{pH} < 3$). Unfortunately, Ramtoola fails to provide teachings or suggestions that cure the deficiencies of Trinh. Once again, if one of ordinary skill in the art were to carefully consider the teachings of both Ramtoola and Trinh, one of ordinary skill in the art would still have no expectation, much less a reasonable expectation, that a hypothetical combination would result in a nanoparticle, wherein the active ingredient is largely contained in a nanoparticle matrix network, and the cyclic oligosaccharide molecules are located on the surface of the nanoparticles. The reason for this is simple---both of Ramtoola and Trinh fail to teach or suggestion this affirmatively claimed aspect o the invention. This utter failure by both references to provide relevant disclosure on this point demonstrates the surprising discovery by the Applicants concerning this claimed aspect. This failure also renders the hypothetical combination of Trinh with Ramtoola non-enabling, as in the case of Trinh and Chin. Moreover, the hypothetical combination of Trinh with Ramtoola would not result in a nanoparticle as, according to Ramtoola, the polymer and the active compound must present complementary ionic forms. As a consequence, the rejection based on the hypothetical combination of Trinh with

Ramtoola must fail. The Applicants accordingly respectfully request withdrawal of the rejection of Claims 1, 2 and 4 – 26 based on the hypothetical combination of Trinh with Ramtoola.

In addition, the Applicants accordingly respectfully submit that the invention concerns all kind of active compounds (hydrophobic, amphiphilic, insoluble and soluble compounds) and is not based on an ion pair mechanism during the preparation process.

In light of the foregoing, the Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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